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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NORRIS, MCLAUGHLIN & MARCUS, PA 875 THIRD AVENUE 18TH FLOOR NEW YORK, NY 10022				
EXAMINER LU, FRANK WEI MIN				
ART UNIT			PAPER NUMBER	
1634				

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/647,002	Applicant(s) KOLTERMANN ET AL.	
	Examiner Frank W. Lu	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 30 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 7-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 16-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/2003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-8 and 16-18 in the reply filed on May 30, 2006 is acknowledged. The traversal is on the ground(s) that "[R]egarding the traversal, Applicants believe that the subject matter of all of claims should be examined together, and that there is no need for a divisional application. In this regard, Applicants believe claims 9-15 have been designated as a separate group because they do not include the wording 'with no sequence determination needed.' Such language has been added to these claims, and, thus, they are believed properly examined with the remaining claims".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the restriction requirement so that Groups I and II will be examined together. First, the restriction is not based on that "claims 9-15 have been designated as a separate group because they do not include the wording 'with no sequence determination needed.'." as argued by applicant. Second, as shown in previous office action, the restriction is based on that different and distinct searches will have to be performed for Groups I and II. For example, the search required for Group I such as step (c) of claim 18 is not required for Group II while the search required for Group II such as step (c) of claim 10 is not required for Group I. Therefore, the requirement is still deemed proper and is made FINAL. Claims 1-8 and 16-18 will be examined.

Specification

2. The disclosure is objected to because of the following informalities: (1) although applicant claims priority for U.S provisional application 60/405,650 in Oath and declaration,

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there is no U.S provisional application 60/405,650 in the first sentence of the specification; and
(2) although there are Figures 5A to 5C, Brief Description of the Drawings of the specification only describes Figure 5.

Appropriate correction is required.

Claim Objections

3. Claim 4 is objected to because of the following informalities: “;” in step (d) should be a period.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-8 and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1, 7, and 16 are rejected as vague and indefinite. Since the specification defines “randomization” as “the manipulation of polynucleotides by unpredicted, stochastic replacements of the original nucleotide at a position with any other nucleotide” (see page 12, last paragraph) while word “selectively” means to choose something and is predicted, selectively and randomizing have opposite meanings and cannot used together. Therefore, it is unclear what means “selectively randomizing”. Please clarify.

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7. Claim 5 is vague and indefinite. Since the phrase “steps (a) to (d), steps (a) to (b) and/or steps (c) to (d) are carried out for multiple cycles” means performing steps (a) to (d) together, steps (a) to (b) together and/or steps (c) to (d) together for multiple times and steps (a), (b), (c), and (d) are each method step, it is unclear what means that steps (a) to (d), steps (a) to (b) and/or steps (c) to (d) are carried out for multiple cycles before entering into a next step. Please clarify.

8. Claim 17 is rejected as vague and indefinite. Since the specification defines “randomization” as “the manipulation of polynucleotides by unpredicted, stochastic replacements of the original nucleotide at a position with any other nucleotide” (see page 12, last paragraph) while word “specifically” means in distinction from others and is predicted, specially and randomizing have opposite meanings and cannot be used together. Therefore, it is unclear what means “randomizing the polynucleotide sequence specifically at these sites at which these variants differ from each other”. Please clarify.

9. Claim 18 recites the limitation “the population of polynucleotides” in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no phrase “population of polynucleotides” in steps (a) to (d) of the claim. Please clarify.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

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international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-8 and 16-18 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Patten *et al.*, (US Patent NO. 6,335,160 B1, filed on December 18, 1996).

Regarding claims 1-8, Patten *et al.*, teach providing at least one polynucleotide having at least one differing site and randomizing the polynucleotides (ie., fragmenting randomly) at or in a proximity to the at least one differing site as recited in claim 1 wherein the polynucleotide is double-stranded and is derived from at least one starting single-strand polynucleotide or is a heteroduplex generated from at least two polynucleotides that differ in at least one site from each other as recited in claim 2 and the polynucleotides or their corresponding translational products are pre-selected with respect to their genotypic and/or phenotypic features as recited in claim 3, further comprises the following steps : (a) providing polynucleotides that differ at one or more sites from each other, whereby these differing sites define start points for randomization; (b) generating heteroduplices from these polynucleotides; c) recognizing resulting mismatching sites; (d) selectively randomizing the polynucleotide at or in proximity to these mismatching sites as recited in claim 4 wherein steps (a) to (d), steps (a) to (b) and/or steps (c) to (d) are carried out for multiple cycles as recited in claim 5, the at least one differing site of the polynucleotide consists of one or more mutations, and the mutations comprise (i) one or more nucleotide substitution (s), (ii) one or more nucleotide insertion (s), (iii) one or more nucleotide deletions), or (iv) a combination of (i) to (iii) as recited in claim 6, further comprises selection or screening for at least one randomized polynucleotide or its corresponding translational products towards a desired property as recited in claim 7, the method of claim 1 is carried out

cyclically (ie., repeating method steps taught by Patten *et al.*,) as recited in claim 8, providing variants of the polynucleotide sequence having at least one differing site and randomizing the polynucleotide sequence at or in proximity to the differing sites as recited in claim 16 (see columns 1-7 and columns 105-110).

Regarding claim 17, Patten *et al.*, teach providing variants from this polynucleotide sequence; randomizing the polynucleotide sequence at these sites at which these variants differ from each other; and selecting or screening a randomized pool of polynucleotides for desired properties (see columns 1-7 and columns 105-110).

Regarding claim 18, Patten *et al.*, teach (a) introducing stochastically random mutations into polynucleotides; (b) selecting or screening the population of polynucleotides generated in step (a); (c) isolating those polynucleotides which encode gene products with improved characteristics; (d) randomizing the polynucleotides at or in proximity to those site(s), at which the polynucleotide isolated in step (c) differ from each other; e) selecting or screening a population of polynucleotides generated in step (d); (f) isolating those polynucleotides which encode gene products with further improved characteristics, in the above method steps (a) to (c) and/or steps (d) to (f)a and/or steps (a) to (9 are optionally repeated iteratively (see columns 1-7 and columns 105-110).

Therefore, Patten *et al.*, teach all limitations recited in claims 1-8 and 16-18.

Conclusion

12. No claim is allowed.
13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

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such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746.

The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

August 4, 2006



FRANK LU
PRIMARY EXAMINER